



PATENT

Our Docket: P-LA 45

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of)

Border and Ruoslahti)

Serial No.: 08/349,479)

Filed: December 2, 1994)

For: INHIBITING TRANSFORMING
GROWTH FACTOR β TO PREVENT
ACCUMULATION OF EXTRACELLULAR
MATRIX)

Assistant Commissioner of Patents
Washington, D.C. 20231
Attn: Box AF

) Art Unit: 1804

) Examiner: S. Ziska

) I hereby certify that this correspondence is being
) deposited with the United States Postal Service as
) first class mail in an envelope addressed to:
) Assistant Commissioner for Patents, Attn: Box AF,
) Washington, D.C. 20231, on October 1, 1996.

By Gregory P. Einhorn
Gregory P. Einhorn, Esq.

October 1, 1996
Date of Signature

DECLARATION UNDER 37 C.F.R. § 1.131

Sir:

1. I, Wayne Border, am a coinventor named on the above-identified patent application, which claims priority to an application originally filed on October 3, 1989.

2. Dr. Erkki Rouslahti and I are coinventors on the above-identified application and we conceived the claimed invention in the United States of America prior to April 14, 1989, which is the date that the article by MacKay, et al., *J. of Clin. Inves.* 83:1160 (April, 1989) (hereinafter "MacKay"), was available to the public; and prior to May, 1989, which is the date that the article by Connor, et al., *J. of Clin. Invest.*

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83:1661-1666 (May, 1989) was published. MacKay and Connor are attached hereto as Exhibit A and B, respectively.

3. As evidence that we conceived of the invention prior to the publication dates of the articles listed in paragraph 2, above, we have enclosed as Exhibits C and D, photocopies of laboratory notebook pages, the dates of which have been redacted but which are prior to April 1, 1989;

a. Exhibit C containing three notebook pages,, each page showing a protocol used in the development of a rabbit anti-TGF- β antiserum used in the invention. The protocol included the injection of linear and cyclic TGF- β peptides.

b. Exhibit D containing three laboratory notebook -- pages demonstrating experiments performed prior to April 1, 1989, the experiments designed to characterize the ability of TGF- β inhibitory agents to decrease the secretion, i.e., accumulation, of extracellular matrix components, specifically, decorin and biglycan. A rat glomerular culture experimental model was used as described in the Specification of the above-indicated application, on pages 16 to 17, Example III(a), entitled "Induction of Experimental

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Glomerulonephritis;" and pages 18 to 19, Example III(c), entitled "Glomerular Culture." Page 1 of Exhibit D shows a laboratory notebook page demonstrating the ability of anti-TGF- β antibody to inhibit the secretion of proteoglycans in the above-described rat glomerular culture model. After addition of the anti-TGF- β antibody to the glomerular cultures, basically as described in the Specification on pages 20 to 22, Example IV and pages 23 to 24, Example VII, extracellular matrix components were isolated and identified by polyacrylamide gel electrophoresis (SDS-PAGE). The glomerular cultures had been metabolically labeled with ^{35}S -methionine, as described in Example II(1) of the Specification, and the amounts of proteoglycans in the gels were analyzed by laser densitometry. Page 2 of Exhibit D shows a laboratory notebook page demonstrating ability of RGD peptides to inhibit the secretion of proteoglycans in a rat glomerular cell culture model. This experiment was designed essentially the same as described above for the anti-TGF- β antibody inhibition experiment, except that glomerular cell cultures were used and RGD peptide was used to inhibit the accumulation of proteoglycan. Page 3 of Exhibit D shows a laboratory notebook page demonstrating ability of platelet derived growth factor

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(PDGF) to inhibit the secretion of proteoglycans in a rat glomerular cell culture model. This experiment was designed essentially the same as described above for the anti-TGF- β antibody inhibition experiment, except that glomerular cell cultures were used and PDGF was used to inhibit the accumulation of proteoglycan.

4. I do not know and do not believe that the invention was in the public prior to the time we conceived of the invention and reduced it to practice and we have never abandoned the application.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may

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jeopardize the validity of the application or any patent issuing therefrom.

Respectfully submitted,

Oct 1, 1996

Date

Wayne Border

Wayne Border